Section 1. Scientific Abstract

The annual incidence of squamous cell carcinoma of the head and neck (SCCHN) in the USA is about 42,000 cases, being about 5% of the total incidence of cancer[1], and having an annual mortality rate of about 12,300 patients[2]. A third of patients present with early-stage disease, of which 60-90% are disease-free at 2-5 years following surgery or radiotherapy[3,4]. The remaining two thirds of patients present with advanced stage disease, of which 20% of patients survive about 1 year, but the median survival is 6 months[5]. The objectives of the clinical program are to conduct a Phase IIa trial of a combined cytokine plasmid-based therapeutic (gene medicine) for the treatment of SCCHN and to monitor for tumor responses attributable to treatment. The genes selected for use in the trial code for human interferon alpha (hIFN-α) and human interleukin-12 (hIL-12) respectively. In pre-clinical trials conducted by the investigators of our laboratory program, this gene combination effectively induced clinically significant tumor immunity in several murine tumor models. The individual cytokine plasmid-based therapeutics, delivered using polymer mediated DNA transfection, are currently being used in two Phase IIa clinical trials in the USA (approved RAC Protocol numbers 9907-330 and 9809-266), and found to be without toxicity.

The proposed Phase IIa trial is a dose escalation study designed to evaluate the safety, and identify any toxicities, associated with the direct injection of formulated plasmid DNA coding for hIFN-α and hIL-12 into patients with squamous cell carcinomas of the head and neck. The trial is designed in two parts. In the first part, (Phase I), safety and tolerability will be evaluated for escalating doses of the cytokine combination. In the second part, (Phase II), the maximum safe dose identified in the Phase I portion of the study will be evaluated using a Gehan design, efficacy variables include tumor size, tumor response and presence (or absence) of development of progressive disease.